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EXAMINER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/966,441	Applicant(s) SZYMCZAK ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/28/01 & telephonic interview 9/20/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *6,18,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _ is/are allowed.

6)☒ Claim(s) *1-5, 7-17, 19-26* is/are rejected.

7)☒ Claim(s) *1-3,5,14,15,17 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. This application contains claims directed to the following patentably distinct species of the claimed invention: bisacodyl, famotidine, prucalopride, diphenoxylate, loperamide, lactase, mesalamine, bismuth, acetaminophen, ibuprofen, naproxen, ketoprofen, cyclobenzaprine, meloxicam, rofecoxib and celecoxib..

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 4 and 16 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the

prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

2. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

3. During a telephone conversation with Timothy E. Tracy on September 20, 2002 a provisional election was made to elect famotidine as the elected species. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6, 18, 27 and 28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

4. The abstract of the disclosure is objected to because of typographical error such as "famotadine" is present in page 7, line 16. Applicant is requested to correct "famotadine" with "famotidine".

Claim Objections

5. Claims 5 and 17 are objected to because of the following informalities: Typographical error such as "famotadine" is present. Applicant is requested to correct "famotadine" with "famotidine".

6. Claim1-3, 14-15 and 26 are objected to because of the following informalities: Term " adsorbant" appears to be an idiomatic English terminology for "adsorbent".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 9-10, 14-15, 23-24 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 lacks antecedent basis for term "silicified microcrystalline cellulose" and "magnesium aluminometasilicate" in claim 1. Similarly claim 10 which is a dependent claim of claim 9 is rejected under 35 USC 112, second paragraph as being dependent on rejected claim.

Claims 14-15 recites the limitation "absorbent" or "absorbant" in 13. There is insufficient antecedent basis for this limitation in the claim. Similarly claim 26 lacks antecedent basis for term "absorbent" in claim 26.

Claims 23-24 lack antecedent basis for term "the composition" in claim 13.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens et al. (US 5679376 A).

In respective to claims 1-2,

Stevens teaches a solid oral dosage form comprising loperamide, simethicone, microcrystalline cellulose and colloidal silicon dioxide, wherein a ratio of simethicone and microcrystalline cellulose is about 1:2.12 (125mg:265.5mg) or a ratio of simethicone and a combination of colloidal silicon dioxide and microcrystalline cellulose is about 1:2.37 (125mg:297mg). See table in column 9, page 65 thru column 10, page 10.

Although the reference is silent about the use of microcrystalline cellulose or colloidal silicon dioxide as an adsorbent, the use of microcrystalline cellulose as a diluent, adsorbent, lubricant or disintegrant or the use of colloidal silicon dioxide as an adsorbent, glidant or disintegrant is notoriously known for the skilled artisan. In other words, such adsorbent characteristic of microcrystalline cellulose or colloidal silicon dioxide must be an inherent function of microcrystalline cellulose or colloidal silicon dioxide . Since the claims do not recite any specific adsorbent(s) (alone or in combination) in a composition, the referenced microcrystalline cellulose or the combination of microcrystalline and colloidal silicon dioxide falls within the broadly defined term "adsorbant" or "adsorbent" (see the definition of term "adsorbant" in page 10, lines 1-5 of the specification). Thus, the reference clearly anticipates the claimed invention.

Regarding the claimed ratio of simethicone to adsorbent "at least about 1:2.22" in claim 1 and "at least about 1:2.00", the referenced ratio of 1:2.12 (simethicone to

microcrystalline cellulose) or 1:2.37 (simethicone to the combination of microcrystalline cellulose and colloidal silicon dioxide) clearly anticipates the claimed ratio.

In respective to claims 4-5,

Stevens expressly teaches that active ingredients for said solid oral dosage form are selected from the group consisting of cimetidine, ranitidine, famotidine, diphenoxylate, loperamide and loperamide-N-oxide (abstracts and claims).

Although famotidine and diphenoxylate are not specifically named in Examples, one of ordinary skill in the art must be able to be "at once envisaged" from the small number of disclosed species. Therefore, the reference clearly anticipates the claimed invention.

9. Claims 1-2, 4-5, 7-8 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Luber et al. (US 6103260 A).

In respective claims 1-2,

Luber teaches an antifoam oral solid dosage form preparations formed from a free glowing granular composition comprising an admixture of simethicone and and either one or both of granular anhydrous tribasic calcium phosphate or dibasic calcium phosphate, wherein the simethicone is adsorbed by the granular anhydrous tribasic or dibasic calcium phosphate or mixture thereof; and wherein ratios of simethicone to granular tricalcium phosphate are 1:3.5 in Examples 1-2 and 1:4 in Example 6.

Although Luber is silent about the use of granular anhydrous tribasic calcium phosphate or dibasic calcium dibasic calcium phosphate as an adsorbent, "adsorbing"

characteristic of "granular anhydrous tribasic or dibasic calcium phosphate or mixture thereof to from the free-flowing granular composition" reads on broadly defined term "adsorbant". The instant specification defines that the term "adsorbant" means a solid material or combination of solid materials that is capable of adsorbing and carrying an oily or fluid material, such as simethicone, while retaining sufficient flowability to assure content uniformity and sufficient compactability to be processed into tablets using direct compression methods (page 10, lines 1-5). Since the claims do not recite any specific adsorbent(s) in a composition, the referenced granular anhydrous tribasic or dibasic calcium phosphate or mixture falls within the broadly defined "adsorbant" or "adsorbent". Thus, the reference clearly anticipates the claimed invention.

Regarding the claimed weight ratio of simethicone to "adsorbant" such as "at least about 1:2.22" or "at least about 1:2.00", the referenced examples clearly falls within the claimed ratio. Therefore, the reference clearly anticipates the claimed invention.

In respective to claims 4-5,

Stevens also teaches that said oral solid dosage form further comprises additional active ingredients selected from H2 receptor antagonists (i.e., famotidine) and antidiarrehal agents (i.e., loperamide and diphenoxylate). See claims 7-8 and column 5, lines 18-21. One of ordinary skill in the art must be able to be "at once envisaged" from the small number of disclosed species. Therefore, the reference clearly anticipates the claimed invention.

In respective to claims 7-8,

Stevens also teaches that the amount of simethicone in the final composition is 10% to 70%, typically 10% to 50% (column 3, lines 39-40 and column 4, lines 45-50). Since the referenced simethicone concentration falls within the claimed "at least 30% wt simethicone" in claim 7 or "from about 31 wt% to about 35 wt% simethicone" in claim 8, the reference clearly anticipates the claimed invention.

In respective to claims 11-12,

Stevens also teaches various ranges of "Hardness" (i.e., 8-10 kp in Example 3; 11-12 kp in Example 4; 8-9 kp in Example 5; 6-14kp in Example 6). Since the referenced "Hardness" value falls within the claimed "a hardness value of at least 2 kp/cm2" and "a harness value of from about 5 to about 10 kp/cm2", the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 3, 9-10, 13-15, 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitsusho Yakuhin Kogyo KK (JP 398241) in view of Tobyn et al. (International Journal of Pharmaceutics 169 (1998) 183-194).

The claims read on a composition comprising an admixture of simethicone, silicified microcrystalline cellulose, and magnesium aluminometasilicates. Further limitations include a) the specific weight ratio of simethicone to a combination of silicified microcrystalline cellulose and magnesium aluminometasilicates; b) the specific concentration of simethicone; c) the specific dosage concentrations of silicified microcrystalline cellulose and magnesium aluminometasilicates; and d) a hardness value of a tablet.

Kitsusho Yakuhin Kogyo KK teaches a method for preparing simethicone tablets by mixing and granulating simethicone with magnesium aluminum metasilicate. In particular, the formulation disclosed by the above Japanese patent requires at most 25%

simethicone and 75% or greater silicate, binder (i.e., starch and lactose) and dispersing agents (i.e., carboxymethylcellulose). Further, the reference teaches that when the amount of simethicone exceeds 25%, there is tendency that a portion of the simethicone can be carried away, therefore the tablet workability is not desirable.

Tobyn discloses the advantage of using silicified microcrystalline cellulose in improving tablet workability such as "powder flow", "tablet strength", "lubricant sensitivity" and "wet granulation" (page 184, column 2, lines 4-9; page 193, column 2, lines 43-48).

The teaching of Kitsusho Yakuhin Kogyo KK differs from the claimed invention in i) the incorporation of silicified microcrystalline cellulose in said composition; ii) "at least 30 wt% simethicone" in said composition; iii) the specific amounts of silicified microcrystalline cellulose and magnesium aluminometasilicates in said composition; and iv) the specific harness value of the tablet. To incorporate such teaching into the teaching of Kitsusho Yakuhin Kogyo KK, would have been obvious in view of Tobyn who teaches the advantage of using silicified microcrystalline cellulose as a pharmaceutical excipients to improve powder flow characteristic, lubricant sensitivity, tablet strength and better bulk physical properties.

One having ordinary skill in the art would have been motivated, with a reasonable expectation of success, to incorporate silicified microcrystalline cellulose having good free-flowing and disintegrating properties (which is relatively new pharmaceutical excipients in the art) such that the tablet workability would be significantly improved. Furthermore, one having ordinary skill in the art would have been motivated to increase

the amount of simethicone above 25% in the solid final blend for tabletting by incorporating silicified microcrystalline cellulose in said composition.

Although the prior art references are silent about the specific dosage amounts of active ingredients and the hardness value of tablet, the optimization of amounts of kwon active and inactive ingredients in a composition or the determination of optimum hardness value of the tablet is well considered within the skill of the artisan, absent evidence to the contrary.

11. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitsusho Yakuhin Kogyo KK (JP 398241) in view of Tobyn et al. (International Journal of Pharmaceuitcs 169 (1998) 183-194) and Stevens et al. (US 5679376).

The modified teaching of Kitsusho Yakuhin Kogyo KK includes all that is recited in claims 16 and 17 except for the incorporation of active pharmaceutical ingredients such as famotidine. Stevens teaches or suggests the use of simethicone and other pharmaceutical excipients in preparing oral solid dosage form containing H2 blockers (e.g,, famotidine). One having ordinary skill in the art would have known that simethicone is routinely combined with H2 blokers such as famotidine in solid oral dosage formulation art, and would have been motivated to further modify the teaching of Kitsusho Yakuhin Kogyo KK such that the better solid oral dosage form containing famotidine would be formulated. One having ordinary skill in the art would have been motivated to do this so that the tablet workability would be significantly improved.

Conclusion

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600

zohreh fay